

## WHAT IS CLAIMED IS :

1. A transgenic fish selected from the group consisting of zebrafish and medaka comprising at least one transgenic DNA sequence capably and competently regulating the expression of and/or encoding a transgenic gene product, wherein the transgenic gene product comprises at least one of an ablation-promoting moiety or a coupled expression system comprising an ablation-promoting moiety and a reporter moiety, wherein the ablation-promoting moiety comprises at least one component of a pro-drug conversion system and wherein the reporter moiety allows selective detection of cells expressing the reporter moiety and whereby the transgenic DNA sequence is heritable by virtue of its stable integration into the genome of said transgenic fish such that the transgenic DNA sequence is propagated through the germline of the transgenic fish and those progeny that inherit the transgenic DNA sequence, and all subsequent progeny derived therefrom that inherit the transgenic DNA sequence, capably and competently express the transgenic gene product in a reproducible spatial and temporal expression pattern.

2. A transgenic fish in accordance with Claim 1 wherein the transgenic fish is a zebrafish.

3. A transgenic fish in accordance with Claim 1 wherein the transgenic fish is a medaka.

4. A transgenic fish selected from the group consisting of zebrafish and medaka in accordance with Claim 1 wherein the regulatory DNA sequence is operably linked to a sequence encoding the gene product(s) such that the regulatory DNA sequence confers specific expression of the gene product(s) in at least one of a specific cell, cell type(s), and/or tissue(s).

5. A transgenic fish in accordance with Claim 4 wherein the transgenic fish is a zebrafish.

6. A transgenic fish in accordance with Claim 4 wherein the transgenic fish is a medaka.

7. A transgenic fish selected from the group consisting of zebrafish and medaka in accordance with Claim 4 whereby the specific cell, cell type(s), and/or tissue(s) wherein the transgene product is expressed in one of a neuron, neuronal cell type(s), and/or neural tissue(s), respectively.

8. A transgenic fish selected from the group consisting of zebrafish and medaka in accordance with Claim 4 whereby the specific cell, cell type(s), and/or tissue(s) wherein the transgene product is expressed in skeletal and/or cartilaginous tissue(s).

9. A transgenic fish selected from the group consisting of zebrafish and medaka in accordance with Claim 4 whereby the specific cell, cell type(s), and/or tissue(s) wherein the transgene product is expressed in one of a heart cell, heart cell type(s), and/or heart tissue(s), respectively.

10. A transgenic fish in accordance with Claim 4 wherein the regulatory DNA sequence which confers at least one of a specific cell, cell type(s), and/or tissue(s) specific expression of the gene product(s) comprises a homologous expression sequence derived from the fish utilized to create the transgenic fish.

11. A transgenic fish in accordance with Claim 4 wherein the regulatory DNA sequence which confers at least one of a specific cell, cell type(s), and/or tissue(s) specific expression of the gene product(s) comprises heterologous expression sequences derived from a species other than the fish utilized to create the transgenic fish.

12. A method of making a transgenic fish of Claim 1 comprising: introducing transgenic DNA sequence into a fish egg cell or embryonic cell wherein the transgenic DNA sequence or some portion of the transgenic DNA sequence is stably integrated into the genome of the egg, cell, or subsequent cells derived thereof, such that the resultant fish embryo develops into an adult transgenic fish capable of germline propagation of the integrated transgenic DNA sequence to its progeny and establishing a stable transgenic line capable of expressing the transgene product of the DNA sequence.

13. A method of determining the inherent regenerative capacity of transgenic fish of Claims 4, 7, 8, and 9 with respect to ablation and subsequent regeneration, or deficiency thereof, of specific targeted cells and/or tissue types comprising a targeted cellular ablation and subsequent regeneration screening procedure whereby the transgenic fish is exposed to an ablation-promoting pro-drug, whereby a cell(s) of the transgenic fish expressing a pro-drug converting moiety is contacted with the pro-drug and wherein the pro-drug is converted into a cytotoxic drug by action of the pro-drug converting moiety and whereby only the cell(s) expressing the pro-drug converting moiety are ablated by action of the drug and, whereby subsequent regeneration, or lack of regeneration, of the ablated cell(s) is detected by the general presence, or absence, of regenerating cells and/or the presence, or absence, of a cellular reporter expressed by regenerating cells, such that if regeneration is detected the fish is determined to be regeneration-competent with regards to the targeted cell(s), cell type(s), or tissue(s) and, whereas if regeneration is not detected the fish is determined to be regeneration-deficient.

14. A method of determining the inherent regenerative capacity of transgenic fish of Claims 4, 7, 8, and 9 with respect to ablation and subsequent regeneration, or deficiency thereof, of cells ablated regionally comprising: a regional cellular ablation and subsequent regeneration screening procedure whereby the transgenic fish is exposed to an ablation-promoting pro-drug, whereby a cell(s) of the transgenic fish expressing a pro-drug converting moiety is brought into contact with the pro-drug and wherein the pro-drug is converted into a cytotoxic drug by action of the pro-drug converting moiety and whereby the cell(s) producing the cytotoxic drug, as well as cells in the general vicinity of the cytotoxic drug producing cell, are ablated by action of the drug and, whereby subsequent regeneration, or lack of regeneration, of the ablated cell(s) is detected by the general presence, or absence, of regenerating cells and/or the presence, or absence, of a cellular reporter expressed by regenerating cells, such that if regeneration is detected the fish is determined to be regeneration-competent with regards to the regionally ablated cell(s), cell type(s), or tissue(s) and, whereas if regeneration is not detected the fish is determined to be regeneration-deficient.

15. A method of identifying genes and genetic mutations affecting cellular regeneration in transgenic fish of Claims 4, 7, 8, and 9 comprising creating and identifying mutant transgenic fish whereby progeny of mutagenized transgenic fish of Claims 4, 7, 8, and 9 are subjected to targeted or regional cellular ablation within the context of a "forward genetics" mutagenesis screen and mutant transgenic fish are identified by an alteration in the competency or deficiency for cellular regeneration in those progeny containing the mutation(s) from mutagenized transgenic fish, such that genetic mutations are identified which alter the regenerative capacity of the fish, whereby mutations either diminish the regenerative capacity of regeneration-competent fish, or enhance the regenerative capacity of regeneration-deficient fish with respect to the ablated cell(s) or tissue types by detecting the presence or absence of regenerating cells and/or the presence or absence of a cellular reporter expressed by regenerating cells, and whereby instances of altered regenerative capacity are due to a mutation(s) that causes an alteration in gene structure, gene product structure, gene product function, and/or gene product expression, thereby identifying the altered gene and/or gene product as a factor capable of influencing the process of cellular regeneration, whereby mapping, cloning, and sequencing of the altered gene identifies a precise genetic alteration capable of influencing the function of the associated gene(s) and thereby the process of cellular regeneration.

16. A method for identifying compounds which alter cellular regeneration in fish comprising a pharmacological screen where transgenic fish of Claims 4, 7, 8, and 9, and mutant fish derived thereof with an altered capacity for cellular regeneration, are subjected to targeted or regional cellular ablation, and subsequently the fish are maintained in the presence of a discrete molecular compound or sets of molecular compounds, such that compounds can be identified which alter the regenerative capacity of the fish, relative to fish maintained in control conditions, whereby compounds either diminish the regenerative capacity of regeneration-competent fish, or enhance the regenerative capacity of regeneration-deficient fish with respect to the ablated cell(s) or tissue types by detecting the presence or absence of regenerating cells and/or the presence or absence of a cellular reporter expressed by regenerating cells, whereby compounds promoting an enhanced capacity for regeneration are

determined to be target compounds and/or drugs capable of promoting the process of cellular regeneration and compounds promoting a diminished capacity for regeneration are determined to be target compounds and/or drugs capable of promoting the process of cellular degeneration.

17. A method in accordance with Claims 13, 14, 15, and 16 where the transgenic fish is zebrafish.

18. A method in accordance with Claim 13, 14, 15, and 16 where the transgenic fish is medaka.